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Near-infrared spectroscopy measurements of cerebral oxygenation in newborns during immediate postnatal adaptation

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Abstract: **OBJECTIVE:** In view of growing concerns regarding the optimal supplementation of oxygen at birth, we measured cerebral oxygenation during the first minutes of life. **STUDY DESIGN:** Using near-infrared spectroscopy, changes in cerebral oxygenated hemoglobin (O(2)Hb), deoxygenated hemoglobin (HHb), and tissue oxygenation index (TOI) were measured during the first 15 minutes of life in 20 healthy newborn infants delivered at term by elective cesarean section. **RESULTS:** O(2)Hb and TOI increased rapidly within the first minutes of life (median slope for O(2)Hb, 3.4 micromol/L/min; range, 1.4 to 20.6 micromol/L/min; median slope for TOI, 4.2 %/min; range, -0.4 to 27.3%/min), and cerebral HHb decreased (median slope, -4.8 micromol/L/min; range, -0.2 to -20.6 micromol/L/min). O(2)Hb, TOI, and HHb all reached a plateau within 8 minutes. **CONCLUSIONS:** A significant increase in cerebral O(2)Hb and TOI and a significant decrease in HHb occur during immediate adaptation in healthy term newborns, reaching a steady plateau at around 8 minutes after birth.

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Changes in cerebral oxygenation in newborns during immediate postnatal adaptation as measured by near-infrared spectroscopy

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Abbreviations

O ₂ Hb	Cerebral oxygenated hemoglobin concentration
HHb	Cerebral deoxygenated hemoglobin concentration
TOI	Tissue oxygenation index ($O_2Hb/[O_2Hb+HHb] \times 100$)
THI	Tissue hemoglobin index
FTOE	Fractional cerebral tissue oxygen extraction $(SAT - TOI)/SAT$
HR	Heart rate
SpO ₂	Peripheral arterial saturation
NIRS	Near-infrared spectroscopy

Key words

Tissue oxygenation index – newborn infants – neonate – non-invasive monitoring – neonatal brain

Short title

Changes in cerebral oxygenation after birth using NIRS

Abstract

Objectives: Little information exists regarding the changes in cerebral oxygenation immediately after birth. In view of growing concern regarding the optimal supplementation of oxygen at birth, this study aimed at gaining more in-depth insight in cerebral oxygenation during the first minutes of life. **Study design:** Using near infrared spectroscopy, the changes in cerebral oxyhemoglobin (O₂Hb), dexoxyhemoglobin (HHb) and tissue oxygenation index (TOI) were measured during the first 15 minutes of life in 20 healthy newborn infants delivered at term by elective caesarean section. **Results:** O₂Hb and TOI increased rapidly within the first minutes of life (median slope O₂Hb: 3.4 μ mol/l/min; range 1.4 to 20.6; median slope TOI: 4.2 %/min; range -0.4 to 27.3), while cHHb decreased (median slope -4.8 μ mol/l/min; range -0.2 to -20.6). O₂Hb, TOI and HHb reached a plateau within 8.0 min and were statistically different from their starting point. **Conclusions:** A significant increase in cerebral O₂Hb and TOI and a significant decrease in HHb can be demonstrated during immediate adaptation in healthy term newborns to reach a steady plateau around 8 minutes after birth. These results provide a better understanding of the normal adaptive changes in cerebral oxygenation in the immediate postnatal period.

Introduction

While there is a substantial body of literature concerning the changes in peripheral arterial oxygen saturation immediately after birth¹⁻³, there is much less available information regarding the changes in cerebral oxygenation during the immediate adaptation. This is of importance considering that worldwide 5-10% of neonates need active resuscitation measures.^{4, 5} While over the last decades, the main focus of concern regarding possible causes of impaired neurological outcome was on insufficient oxygenation during the perinatal period, there is, based on the work of Ola Saugstad, Maximo Vento and other researchers, increasing concern regarding short- and long-term damage to newborns exposed to high oxygen concentrations in the delivery room.⁶⁻¹³ It is only recently that the noxious potential of excess oxygen exposure during the resuscitation of near-term or term infants immediately after birth has been recognized.^{14, 15} It has therefore been proposed to start neonatal resuscitation in the delivery room by administering a lower FiO_2 , a proposal which has been echoed by several international recommendations on neonatal resuscitation.¹⁶⁻¹⁸ There is a growing consensus among neonatologists regarding the need to reduce the FiO_2 in the delivery room, however, the question of the starting FiO_2 value remains a matter of debate.^{19, 20}

Pulse oximetry as non-invasive, continuous technique allows to monitor peripheral arterial oxygenation saturation (SpO_2). In case of measurement over the right hand or wrist, this SpO_2 is representative of the oxygen saturation reaching the brain. Nevertheless, we still lack more precise information about the changes in cerebral tissue oxygenation in the very early postnatal adaptation. Near-infrared spectroscopy (NIRS) is a well described non-invasive technique, taking advantage of the transparency of

biological tissue to light in the near-infrared spectrum, and allows to explore changes in cerebral tissue oxygenation.²¹⁻²⁴ Newer near-infrared spectrometers allow additional measurement of a quantitative tissue oxygenation index (TOI) representing the ratio of O₂Hb in total hemoglobin (O₂Hb/[O₂Hb+HHb]). It has been shown that NIRS is able to monitor cerebral hemodynamics in critically ill term and preterm infants.^{21, 25, 26} In order to get a more in-depth understanding of the physiological changes in terms of cerebral oxygenation, we aimed with this study at understanding how much and in which time frame O₂Hb, HHb, TOI and SpO₂ change in healthy term newborns during the first minutes of life. This knowledge may provide the neonatologist with important information when addressing the issue of optimal oxygen supplementation in the delivery room.

Patients and methods

Neonates born by elective Caesarean section at term were eligible for the study. The exclusion criteria were need for neonatal resuscitation, genetically defined syndromes, congenital malformations, and infants in whom no parental consent or no good quality near-infrared signals could be obtained. At our perinatal center, neonates born by Caesarean section are routinely under supervision of a neonatologist for the first 10-15 minutes after birth. For this study, the newborn infant was placed on a resuscitation table under a radiant warmer with the head in neutral position. The head and the right arm were cleaned from vernix. Using a pulse oximeter (N-200 / N-395, Nellcor INC, USA), arterial oxygen saturation was continuously measured over the right hand or wrist.

Oxyhemoglobin (O₂Hb), deoxyhemoglobin (HHb) and tissue oxygenation index

(TOI) were measured using NIRS (NIRO 300 HamamatsuTM Photonics, Japan). The NIRS-sensor contains one light source (with 775, 810, 850 and 910 nm wavelengths) and one detector with 3 segments (SI-photodiodes). The emitter and receiver optodes were fixed in a probe holder to ensure the inter-optode distance of 50 mm, and the optode was connected to a pre-calibrated measuring unit of the NIRO-300. The chosen path-length of the NIRO was 19 mm, and the optical path-length was 3.8 mm. Interference from light was prevented by shielding the optode, which was placed on the skin overlying the right forehead avoiding the area of the sagittal sinus in order to measure brain tissue oxygenation, and then attached to the baby's head using stretch bandages. NIRS measurements were started as soon as the pulsoximeter probe was secured on the right hand/wrist in order to measure pre-ductal oxygen saturation and heart rate (HR). To avoid any artifacts, the baby was thereafter not disturbed over the next 10 to 15 minutes, excepted for clinical reasons.

All measured data were stored electronically at a sample rate of 2 seconds for subsequent analysis, while demographic data were noted. All NIRS studies were performed by the same investigators who were not involved in the care of the newborns in the delivery room.

Written parental informed consent was obtained prior to each study, and the study was endorsed by the local Ethics Committee of the University Children's Hospital Zurich.

Data analysis

All continuously measured NIRS data were evaluated individually. Fractional cerebral oxygen tissue extraction (FTOE) was calculated as $(\text{SpO}_2\text{-TOI})/\text{SpO}_2$, and

oxygen arterio-venous difference (O_2 -AV-Difference) as SpO_2 -TOI. Median values and the 25th and 75th centiles were calculated for O_2 Hb, HHb, TOI, THI, FTOE, O_2 -AV-Difference, HR and SpO_2 over the whole measurement period, and shown graphically in one minute intervals for the whole group. These values were compared at two time periods: during the first minute of measurement (starting point), and at 8 minutes of measurement (plateau phase). For statistical analysis, the paired Student-t test (StatView version 5.01 for Windows, SAS Inc., Carry, NC, USA) was used. The slope, and therefore the concentration change per minute, was calculated for the part with great concentration changes of all parameters before reaching a turning point, followed by the plateau phase.

Results

All infants were born by uncomplicated elective caesarean section with normal Apgar scores. No infant received medication, and no infant required bag and mask resuscitation. 20 infants had NIRS measurements with the required quality, 3 infants out of these were excluded, 2 for having needed supplemental oxygen over a few minutes, and 1 infant born at 34 3/7 weeks gestation, leaving 17 infants for analysis (8 girls, 9 boys).

The median gestational age was 38 1/7 weeks (range 36 6/7 to 40 2/7 wks), the median birth weight was 3200 g (range 2300 to 4190 g), median umbilical artery pH was 7.30 (range 7.20 to 7.38), median Apgar score values were 8 at 1 minute (range 7 to 9, mean 8.3), 9 at 5 minutes (range 8 to 10, mean 9.1), and 10 at 10 minutes (range 8 to 10, mean 9.6).

The median age at the start of NIRS measurement was 2 minutes after birth (range 1 to 4 min), and SpO₂ measurements were reliable within 1 minute after placing the sensor. Figure 1 depicts the changes of TOI, SpO₂, FTOE, O₂-AV-Difference, THI, HR, O₂Hb and HHb, shown as median values and 25th and 75th centiles for the whole group over the measurement period. The changes in O₂Hb, TOI, SpO₂ and HHb reached a plateau within 8.0 minutes (median; range 6.2 to 11.3 min), and were statistically different from their starting point (O₂Hb: p = 0.0001; TOI: p = 0.0003; HHb: p = 0.00007, SpO₂: p = 0.0007). All other parameters did not show significant changes. Thereafter all parameters remained on their newly reached level. O₂Hb, TOI along with pre-ductal SpO₂ increased rapidly within the first minutes of life (median slope O₂Hb: 3.4 μ mol/l/min; range 1.4 to 20.6; median slope TOI: 4.2 %/min; range -0.4 to 27.3; median slope SpO₂ 4.6 %/min; range 0.2 to 15.3), while HHb concentration decreased (median slope -4.8 μ mol/l/min; range -0.2 to -20.6).

Discussion

We investigated the adaptive changes in cerebral tissue oxygenation during the immediate adaptation from intra- to extra-uterine life in healthy term infants born by elective Caesarean section. We observed a steady increase in cerebral O₂Hb, TOI and SpO₂ until a steady state around 8 minutes of life, with a simultaneous decrease in cerebral HHb. As shown in Figure 1, TOI and SpO₂ tracked each other very closely. Interestingly, FTOE and O₂-AV-Difference remained constant which reliably indicates that oxygen consumption did not change significantly during this time period.

To our knowledge, only two studies so far looked at these changes in the first minutes of life using NIRS. Peebles et al. reported on a single patient²⁷, Isobe and Kusaka measured oxyhemoglobin (HbO₂), deoxyhemoglobin (HHb), total hemoglobin concentration (THb) and hemoglobin oxygen saturation in the brain tissue of 7 term infants immediately after birth.²⁸ Two of these infants were delivered vaginally, three by elective and another two by emergency C-section. One of the latter infants was severely growth retarded. We intended to study infants without any signs of fetal distress and without a history of intrauterine growth retardation in order to approach as much as possible the situation of a normal group of newborns.

No study so far has assessed the changes in brain tissue oxygenation using TOI immediately after birth. In contrast to O₂Hb and HHb which are values relative to the starting point, TOI is an absolute value which can therefore be measured serially in the same patient.²⁹ Naulaers and co-workers measured normal values of TOI over the first 3 days of life in premature infants under 30 weeks gestation, showing a significant increase in median TOI from 57% on day 1 to 76% on day 3, and that this increase was independent of gestational age. They also showed that although NIRS is very sensitive to movement, TOI proved to be less sensitive to movement and very stable with a small standard deviation around 2%. The increase in TOI seems to be at least partially explained by the increase in cerebral blood flow as observed by several authors.^{30, 31}

The optimal FiO₂ during neonatal resuscitation remains a subject of debate. SpO₂ is used in many delivery rooms over the world to titrate the FiO₂ of supplemental oxygen. Against this background, the International Liaison Committee on Resuscitation called for more data to allow evidence-based recommendations to be made regarding the role of pulse oximetry measurements immediately after birth.⁵ Rabi and colleagues

state that pulse oximetry could potentially play a role in adjusting the oxygen concentration beyond 2 minutes of life, but the initial decision on whether to initiate oxygen supplementation should be based on clinical evaluation.² While we fully agree on the second part of this statement, relying on SpO₂ values within the first 7-10 minutes, however, has the potential to lead to an overuse of supplemental oxygen rather than to reduce unnecessary oxygen exposure to a population of patients at risk for oxidant injury. First, SpO₂ changes substantially immediately after birth^{5, 12, 32, 33}, meaning that one would have to know, minute for minute, the normal SpO₂ values to be able to decide based on the actual SpO₂ reading. Second, the wide SpO₂ ranges shown in all studies further complicate the clinician's decision. Furthermore and even more importantly, caution must prevail before assuming that the range of SpO₂ values measured in healthy term and near-term infants also applies to more preterm infants or to sick preterm and term neonates.³ On the other hand, the additional use of a pulse oximeter during the first 10 minutes of life has the advantage of providing a continuous reading of heart rate, and in helping to reduce the oxygen concentration, for instance in infants with tcSO₂ readings $\geq 95\%$.¹⁸

A limitation of our study concerns the fact that our study group does not fully represent the true normal group of newborns. In order to track the changes in cerebral oxygenation immediately after birth, we performed this study in neonates born by elective C-section, well knowing that by doing so we would select a specific group of newborns from a normal collective. We chose this mode of delivery because of ease of access to these newborns immediately after birth. Healthy infants delivered vaginally would admittedly constitute the "true" normal group. Obtainment of ethical clearance, however, would be as difficult as persuading parents to be separated from their healthy

infants for study purposes only. In spite of this limitation, the plateau of steady SpO₂ values in our infants was reached around 8 minutes which is in line with the results of Kamlin.³ Importantly, this same group showed that maternal anesthesia, either spinal or general, did not additionally influence SpO₂.

As shown in this study, using NIRS with TOI allows to extend our knowledge of brain tissue oxygenation by moving from peripheral arterial oxygen saturation into the organ of interest. Although still considered mainly a research tool, NIRS has the potential to provide the clinician with important information in different clinical situations, and to gather important reference values for daily clinical work. As stated by van Bel and co-workers in their review, the present technical state of NIRS-monitored cerebral oxygenation does not attain the required precision to use TOI as a robust quantitative measure²⁴. Nevertheless, this fact does not preclude using TOI as a semi-quantitative variable to monitor trends in cerebral oxygenation in a given patient, as considerable changes in TOI may provide the clinician with important information with regard to choosing a course of action. We agree with these authors that in this light NIRS-monitored TOI, among other variables of cerebral oxygenation, may well be increasingly used in clinical practice in conjunction with the conventional means presently at hands such as pulse oximetry and arterial pO₂

A better understanding of the normal adaptive changes in cerebral oxygenation in the immediate postnatal period is of paramount importance in the light of a more brain-oriented neonatal medicine with on one side insufficient tissue oxygenation, and on the other side undue supplemental oxygen exposure immediately after birth, thereby placing the neonate born from a milieu of physiologic hypoxemia and with an unprepared anti-oxidative defense system at greater risk of impaired outcome. Moreover, this better

understanding should then allow expanding our research by exploring these issues in neonates with a disturbed adaptation process.

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Legend

FIGURE 1: Cerebral O₂Hb, HHb, TOI, THI, FTOE, O₂-AV-Difference, HR and preductal SpO₂ (SAT) presented as median values (thick line) with 25th - and 75th centiles (thin lines) for the whole group during the first minutes of life.

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Figure

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